

Department of Health and

5 6 4 0 5 1

Phase I Grant

Follow instruction

& NAME: RASO, VICTOR A

APPL NO:1 R43 AG15746-01

DUAL: NS RCVD: 09-04-97

IRG: ZRG1-NEUA(1B)

COUNCIL: 01/98

1. TITLE OF APPLICATION (Do not exceed 50 typewriter spaces)
IMMUNOTHERAPY OF ALZHEIMER'S DISEASE

2. SOLICITATION NO. PHS 97-2

3. PRINCIPAL INVESTIGATOR

☐ New Investigator

3a. NAME (Last, first, middle)
RASO, VICTOR A.

3b. DEGREE(S)

B.S.

Ph.D.

☒ SOCIAL SECURITY NO.

Provide on Personal Data Page

3d. POSITION TITLE
SENIOR SCIENTIST

3e. MAILING ADDRESS (Street, city, state, zip code)

BOSTON BIOMEDICAL RES. INST.

20 STANIFORD STREET

BOSTON, MA 02114

BITNET/INTERNET Address:

3f. TELEPHONE AND FAX (Area code, number, and extension)

TEL: (617) 742-2010, x 316

FAX: (617) 523-6649

4. HUMAN
SUBJECTS

4a. If "yes," Exemption no.

or ☐

IRB approval date

☐ Full IRB or
Expedited
Review

4b. Assurance of
compliance no.

5. VERTEBRATE
ANIMALS

5a. If "Yes,"
IACUC
approval
date

5b. Animal welfare
assurance no.

☒ NO
☐ YES

☐ NO
☒ YES

1/2/97

A3177

6. DATES OF PROJECT PERIOD

From: 4/1/98

Through: 8/31/98

7. COSTS REQUESTED

7a. Direct Costs

7b. Total Costs

\$ 92,980

\$ 99,980

8. PERFORMANCE SITES (Organizations and addresses)

Boston Biomedical Res. Inst.

20 Staniford Street

Boston, MA 02114

9. APPLICANT ORGANIZATION (Name and address of applicant
small business concern)

Boston Biotechnology Corp.

20 Staniford Street

Boston, MA 02114

10. ENTITY IDENTIFICATION NUMBER

1042766443A1

Congressional District

11. SMALL BUSINESS CERTIFICATION

☒ Small Business Concern

☐ Women-owned

☐ Socially and Economically Disadvantaged

12. NOTICE OF PROPRIETARY INFORMATION: The information identified
by asterisks(*) on pages

of this application constitutes trade secrets or information that is commercial
or financial and confidential or privileged. It is furnished to the Government
in confidence with the understanding that such information shall be used or
disclosed only for evaluation of this application, provided that, if a grant is
awarded as a result of or in connection with the submission of this application,
the Government shall have the right to use or disclose the information herein
to the extent provided by law. This restriction does not limit the Government's
right to use the information if it is obtained without restriction from another
source.

13. DISCLOSURE PERMISSION STATEMENT: If this application does
not result in an award, is the Government permitted to disclose the title
only of your proposed project, and the name, address, and telephone num-
ber of the official signing for the applicant organization, to organizations
that may be interested in contacting you for further information or possible
investment? ☒ YES ☐ NO

14. OFFICIAL SIGNING FOR APPLICANT ORGANIZATION

Name: Vincent F. Raso

Title: Treasurer

Address: Boston Biotechnology Corp.

20 Staniford Street

Boston, MA 02114

Telephone: (617) 742-2010, (x301)

FAX: (617) 523-6649

BITNET/INTERNET Address:

15. PRINCIPAL INVESTIGATOR ASSURANCE: I certify that the statements
herein are true, complete, and accurate to the best of my knowledge. I am
aware that any false, fictitious, or fraudulent statements or claims may subject
me to criminal, civil, or administrative penalties. I agree to accept responsibility
for the scientific conduct of the project and to provide the required progress
reports if a grant is awarded as a result of this application.

SIGNATURE OF PERSON NAMED IN 3a
(In ink. "Per" signature not acceptable.)

Victor Raso

DATE

8/29/97

16. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete, and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Service terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.

SIGNATURE OF PERSON NAMED IN 14
(In ink. "Per" signature not acceptable.)

Vincent F. Raso

DATE

8/29/97

Abstract of Research Plan

NAME, ADDRESS, AND TELEPHONE NUMBER OF APPLICANT ORGANIZATION

Boston Biotechnology Corporation
 20 Staniford Street, Boston, MA 02114
 617-742-2010

YEAR FIRM FOUNDED

1983

NO. OF EMPLOYEES (include all affiliates)

85

TITLE OF APPLICATION

Immunotherapy of Alzheimer's Disease

KEY PERSONNEL ENGAGED ON PROJECT

| NAME | ORGANIZATION | ROLE ON PROJECT |
|-------------------|----------------------------------|------------------------|
| Victor Raso | Boston Biotechnology Corporation | Principal Investigator |
| Christine Kearney | Boston Biotechnology Corporation | Research Technician |

ABSTRACT OF RESEARCH PLAN: State the application's broad, long-term objectives and specific aims, making reference to the health-relatedness of the project. Describe concisely the research design and methods for achieving these goals and discuss the potential of the research for technological innovation. Avoid summaries of past accomplishments and the use of the first person. This abstract is meant to serve as a succinct and accurate description of the proposed work when separated from the application. If the application is funded, this description, as is, will become public information. Therefore, do not include proprietary or confidential information. DO NOT EXCEED 200 WORDS.

The β -amyloid peptide and the cerebral plaques that it forms are likely either the direct or indirect cause of Alzheimer's disease. This peptide is produced in both the brain and peripheral tissues by cleavage from a common cell-surface precursor protein. Soluble β -amyloid exists free in the blood and cerebrospinal fluid while "insoluble" aggregates are deposited in the brain as amyloid plaques. The soluble and insoluble forms of β -amyloid present within Alzheimer's patients appear to be in dynamic equilibrium. We will displace this equilibrium away from the brain by generating peptide-specific antibodies in a transgenic mouse model of Alzheimer's disease. Restricted to the peripheral circulation, these antibodies will sequester β -amyloid peptide in the blood and by doing so gradually deplete intercommunicating peptide levels in the brain. Decreased concentrations of β -amyloid in the brain should reduce the size and number of brain plaques or delay their appearance. The studies would establish a causal relationship between amyloid deposits and memory impairment in these transgenic mice. Moreover, by virtue of their ability to perturb the soluble β -amyloid equilibrium, our expressly designed β -amyloid antigens and antibodies would form a basis for the immunotherapy of Alzheimer's disease.

Provide key words (8 maximum) to identify the research or technology.

Alzheimer's disease, Antibody, Immunotherapy, Transgenic, Vaccine, β -Amyloid

Provide a brief summary of the potential commercial applications of the research.

The objective of this Phase I project is to test the concept of using immunotherapy to alter the cause of disease in a transgenic mouse model of Alzheimer's disease. The eventual Phase II program will generate clinically useful, and highly specific vaccines for the treatment or prevention of Alzheimer's disease.

Budget for Phase I—Direct Costs Only

FROM
4/1/98TO
8/31/98

| PERSONNEL (Applicant organization only) | | Type Appt. (months) | % Effort on Project | Institutional Base Salary | DOLLAR AMOUNT REQUESTED (omit cents) | | |
|---|--------------------|---|------------------------------|---------------------------------|--------------------------------------|--------------------|-----------|
| NAME | Role on Project | | | | Salary Requested | Fringe Benefits | TOTALS |
| Victor Raso | P.I. | 12 | 100 | | | | |
| | | | | | | | |
| Christine Kearney | Res. Tech. | 12 | 100 | | | | |
| | | | | | | | |
| | | | | | | | |
| | | | | | | | |
| SUBTOTALS → | | | | | 59,120 | 19,510 | 78,630 |
| CONSULTANT COSTS | | | | | | | 0 |
| EQUIPMENT (Itemize) | | | | | | | 0 |
| SUPPLIES (Itemize by category) | | | | | | | 8,350 |
| TRAVEL | | | | | | | 0 |
| PATIENT CARE COSTS | | <input type="checkbox"/> Inpatient <input type="checkbox"/> Outpatient | | | | | |
| CONTRACTUAL COSTS | | | | | | | 0 |
| OTHER EXPENSES (Itemize by category) | | | | | | | 6,000 |
| TOTAL DIRECT COSTS (Also enter on Face Page, Item 7a) → | | | | | | | \$ 92,980 |
| FIXED FEE REQUESTED | | | | | | | \$ 7,000 |

OTHER SUPPORT (see instructions) ☐ NO ☐ YES